

Use of Micronutrients and Alternative Drugs by Children With Acute Lymphoblastic Leukemia

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The use of alternative therapies is thought to be common among cancer patients. To clarify the popularity of micronutrients among children with cancer, we performed a controlled follow-up survey. The use of micronutrients and alternative drugs by 15 families of children with acute lymphoblastic leukemia (ALL) receiving chemotherapy (62 members) and 26 control families (106 members) was monitored by means of daily diaries from November 1987 to December 1989. Forty percent of children with ALL (6 of 15) and 7.7% of their controls (2 of 26) took alternative medicines, the usage among the children with ALL being statistically significantly more common (difference, 32.3%; 95% confidence interval for difference [CI] 7.1–57.5%;

$P < 0.04$). All children with ALL and 50.0% of the control children (13 of 26) took vitamins (difference, 50.0%; 95% CI, 20.4–79.6%; $P < 0.01$). A total of 27.7% of the other members of the ALL families (13 of 47) and 11.1% of their counterparts in the control families (10 of 90) took alternative medicines, the usage in the index families being statistically significantly more common (difference, 16.6%; 95% CI, 3.4–29.7%; $P < 0.03$). The malignancy increased the use of alternative medicines among all members of the family and of vitamins and trace elements among the affected children. **Med. Pediatr. Oncol.** 28:205–208

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INTRODUCTION

The use of alternative medicine has become a common habit, especially among patients with malignancy; in a telephone interview, one third of adult cancer patients reported having used at least one unconventional therapy during the preceding year [1]. Many cancer patients take antioxidant vitamins, even though conflicting results exist regarding their value for preventing or treating cancer [2–6]. The parents of a child with cancer want to help their child to recover from the disease; with this in mind, they provide extra nutrients [7]. There is a reasonable amount of information available on the use of alternative therapies among adult cancer patients [8]. Less is known about children [7,9], however, and surveys with healthy controls are lacking. Micronutrients may cause adverse effects, and it has been suspected that they may enhance the growth of the malignancy [10,11]. Thus, physicians responsible for patients with cancer should know what micronutrients or alternative medicines their patients take during chemotherapy and counsel them accordingly. We evaluated the magnitude of the use of micronutrients and alternative medicines in a controlled survey concerning the whole family.

PATIENTS AND METHODS

Index Families

The series was composed of 15 children (mean age, 7.3 years; range, 4.3–12.6 years) with acute lymphoblastic

leukemia (ALL) at the remission stage who were being treated at the Department of Pediatrics, University of Oulu. Patients were monitored for 9,063 days from November 1987 for as long as the cytostatic therapy continued or to December 1989 for the use of alternative medicines. Thirteen children were in their first remission, 2 children were in their second remission, and 1 child relapsed during the course of monitoring. Most patients had reached the continuation phase of their therapy. One of the investigators took care of the patients during their visits to the outpatient department. Detailed information on the treatment provided is given elsewhere [12]. Eighteen siblings (mean age, 10.6 years; range, 2.8–23.3 years) were monitored for 9,741 days, and 29 parents (mean age, 36.1 years; range, 25.7–48.3 years) were monitored for 17,393 days.

Control Families

The control families were selected at random from schools or family health care centers in Oulu. They were monitored for 1 year, and new controls were selected for the second year. They matched the index families in number of children, children's age and sex, and family socioeconomic status [12]. Twenty-six control children

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of the patients (mean age, 7.0 years; range, 3.9–11.8 years) were monitored for 9,050 days, 29 control siblings (mean age, 9.0 years; range, 1.8–16.1 years) were monitored for 9,692 days, and 61 control parents (mean age, 33.7 years; range, 25.8–50.3 years) were monitored for 1,7741 days. One control family left the study after 7.5 months, and a new one was selected. All other index and control families were followed according to the study plan.

The protocol was approved by the Ethical Committee of the Medical Faculty, University of Oulu, Finland, and informed consent was obtained from the parents.

Each family member listed the medications they were taking in a diary, which was returned by mail every second week. The decisions about the use of vitamins and alternative therapies were made by the parents. The study nurse made sure that all diaries were available. The index children visited the outpatient department every fourth week, and all adults visited every third month. Any family member could visit the outpatient department whenever they needed a physician's (M.M.) or study nurse's examination for infections. The accuracy of the data in the diaries was checked during these occasions. The medicines were classified into vitamins, iron pills, fluoride tablets, minerals, and alternative medicines. The number of days on which these were taken were calculated per person-year at risk and compared between the children with ALL and their controls as well as between the other members of the index and control families.

The differences between the proportions were tested with the standardized normal deviate (SND) test for proportions, and 95% confidence intervals (95% CI) were calculated accordingly [13].

RESULTS

Children with ALL took preparations of multivitamins and trace elements, alternative medicines, fluoride tablets, and other minerals (except for iron tablets) to a statistically significantly greater extent than their controls (Table I). The differences were greatest in the number of days taking multivitamins and trace elements, which the children with ALL took almost daily. Forty percent of children with ALL (6 of 15) and 7.7% of their controls (2 of 26) took one or more alternative medicines, the numbers differing in a statistically significant manner (difference, 32.3%; 95% CI, 7.1–57.5%; $P < 0.04$). Three children with ALL took shark liver tablets, one took oil of evening primrose and carrot biscuits, and four took a mixture of trace elements; one control child took tablets made from kiwi fruits and the other some form of plant extract. The control children took more vitamin C, vitamins A and D, and iron tablets than did patients (Table I). All index children and 50.0% of control children (13 of 26) took vitamins, the numbers differing in a statistically significant

manner (difference, 50.0%; 95% CI, 20.4–79.6%; $P < 0.01$). In addition, the number of days taking all vitamins per person-year at risk were higher among patients than their controls (340.6 vs. 56.9; difference, 283.7; 95% CI, 277.4–288.4; $P < 0.001$).

Thirteen of 47 other members of the ALL families (27.7%) and 10 of their 90 counterparts in the control families (11.1%) took alternative medicines, the usage in the index families being statistically significantly more common (difference, 16.6%; 95% CI, 3.4–29.7%; $P < 0.03$). Children with ALL took them even more than their own family members (Table I). The selection of alternative products was more numerous among the other members of the families, however, and included various plant and vegetable oils, silicon and seaweed products, and many mixed products, without the subject's having any exact knowledge of their content. The siblings of the children with ALL more often took fluoride tablets than their controls. Twenty-three of 47 members of the index families (48.9%) and 24 of their 90 controls (26.6%) took some vitamins, the numbers differing in a statistically significant manner (difference, 22.3%; 95% CI, 5.5–39%; $P < 0.02$). However, the number of days taking all vitamins were statistically significantly lower for the members of the index families than for those of the control families (Table I).

DISCUSSION

Children with ALL took micronutrients and vitamins much more often than their controls. It has been hypothesized that vitamin A has an anticancer effect by controlling cellular differentiation and growth, and that its precursor beta-carotene, vitamin C, vitamin E, and selenium have anticancer effects because of their antioxidant properties [14]. The results of controlled trials on micronutrients and the prevention of cancer are controversial, however, and a large follow-up study showed no reduction in the incidence of lung cancer among male smokers after 5 to 8 years of dietary supplementation with vitamin E or beta-carotene [5]. High doses of vitamins A, B₆, C, and E have been found to reduce the risk of recurrence in patients with transitional cell carcinoma of the bladder receiving bacille Calmette-Guerin (BCG) immunotherapy [6].

The role of vitamins in cancer therapy is just as controversial as their role in its prevention. Retinoic acid seems to be highly effective for inducing complete remission in patients with acute promyelocytic leukemia [15], and a significant improvement in the survival of these patients has been obtained by combining retinoic acid with cytostatics [16]. High doses of vitamin C have failed to have any beneficial effect on the survival of cancer patients [17]. It has been suggested that micronutrients may even have deleterious effects during cancer therapy [10,11].

TABLE I. Numbers of Days Receiving Micronutrients and Alternative Medicines per Person-Year at Risk in the Index and Control Families, With 95% Confidence Intervals for the Differences

Medicine	Index members					Other family members				
	Patient	Control	D	P value	95% CI	Index	Control	D	P value	95% CI
Multivitamins and trace elements	326.7	14.7	312.0	<0.001	306.6–317.6	10.2	16.1	–5.9	<0.001	–6.9–4.7
Vitamin A + D	13.9	38.7	–24.8	<0.001	–27.7–22.3	13.1	20.1	–7.0	<0.001	–8.0–5.5
Vitamin C	0.0	3.5	–3.5	<0.001	–4.3–2.8	1.5	4.7	–3.2	<0.001	–4.0–2.6
Vitamin B	0.0	0.0	0.0	—	—	0.1	1.5	–1.4	<0.001	–1.5–0.9
Alternative medicines	98.0	0.8	97.2	<0.001	94.9–102.2	17.3	10.2	7.1	<0.001	5.8–8.4
Fluoride	180.7	43.8	136.9	<0.001	132.1–141.6	19.0	12.0	7.0	<0.001	5.5–8.0
Iron	0.7	12.0	–11.3	<0.001	–12.8–9.9	0.7	1.1	–0.4	<0.001	–0.7–0.3
Other minerals	9.9	0.0	9.9	<0.001	8.8–10.1	0.1	0.3	–0.2	NS	–0.3–0.04

D = difference; CI = confidence interval; NS = not significant.

Vitamins account for only 0–2.7% of drug prescriptions for children in Sweden and in the United States [18,19]; iron accounts for 0–1% [18]. However, their use is more common because they can be bought freely from any pharmacy. In Finland, 9% of children in 5,858 families interviewed at home in 1987 had taken vitamins or micronutrients during the preceding 2 days [20]. This figure is lower than in our survey, in which the number of days taking all vitamins per person-year at risk among the control children was 56.9. This difference can be explained by the different methods used for collecting the data. In our survey, all children with ALL took vitamins, whereas the corresponding figures were 14% for children with cancer in Australia [7] and 13% for adult cancer patients in Great Britain [8].

Forty percent of children with ALL in our study took alternative medicines, which is a higher figure than in earlier surveys in Australia and the United States [7,9]. Our patients resemble those in Scandinavia very well, because all children with ALL in our study are treated and undergo follow-up according to the same protocols in the five Nordic countries [21]. The parents reported daily use of alternative medicines, and it may be that their use was even more common. This is because the inquiry was being made by the doctor treating the patients at the time, and it has been reported that approximately half of all patients do not inform their doctors of alternative therapies [7,8].

In earlier studies, the consumption of medicines has been estimated from the numbers of prescriptions; thus, our figures for the number of days taking medicines cannot be directly compared with such results. There are data available based on individual and population monitoring systems in which the consumption during the past 48-hour period is reported [18], but to our knowledge there has been no earlier diary survey in which patients have recorded their use of medicines daily. This kind of continuous follow-up undoubtedly gives the most reliable data, but it cannot be done on a large scale, evaluating the use of drugs among whole populations.

The composition of many alternative medicines is unclear, and they do not bear any exact list of ingredients. They are often made of exotic animal products like shark liver or extracts from some plants or vegetables. The number of alternative medicines is growing continuously, and it is impossible to be aware of their contents or of their possible harmful effects. One survey identified a child with cancer who was taking laetrile “vitamin B₁₇” [9], which may actually cause cancer [11]. In our survey and as seen earlier [7], none of the children gave up conventional therapy. As reasons for the alternative therapies, parents stated their desires to cure the cancer, to help the child to cope with the unpleasant treatment, or to help their children feel that they have some control over their disease [7]. Adult cancer patients following alternative therapies have been found to be more anxious than those receiving conventional treatment only [8], and it may be their own anxiety that leads parents to give their children alternative medicines more often than do control parents.

The use of alternative medicines and vitamins among pediatric cancer patients is very common; all children with ALL in our survey took vitamins almost daily, and 40% of them took alternative medicines. Having a child with ALL in the family also increased the use of alternative medicines among other family members. There is much money being spent on alternative medicines that are expensive without having any proven efficacy in the treatment of cancer. Because parents do not always inform physicians about alternative medicines [7,8], a physician should initiate discussion—it is important to know the use of alternative medicines in case of some unexpected side effects. To prevent the rejection of conventional treatment, physicians must remain nonjudgmental. More scientific data are needed on the effects of vitamins and micronutrients on cancer, especially because of their common use.

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